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## ISCHAEMIC HEART DISEASE

**PROVE-IT proves the obvious, but A-Z does not** ► PROVE-IT proved the benefits of atorvastatin 80 mg over pravastatin 40 mg. The Z phase of the A to Z trial randomised 4500 patients who had been admitted to hospital with acute coronary syndrome (ACS) to four months placebo, or 30 days of 40 mg of simvastatin followed by 80 mg for the remainder of a four month period. Following this initial period all patients were switched to 20 mg of simvastatin once a day. Surprisingly, the higher dose regimen failed to show a significant benefit on the primary end points of cardiovascular death, myocardial infarction (MI), re-admission for ACS or stroke at four months (hazard ratio 0.89, 95% CI 0.76 to 1.04;  $p = 0.14$ ), although there was some later benefit from aggressive treatment. Furthermore, side effects were particularly problematic; nine patients developed myopathy and there were three cases of frank rhabdomyolysis. In both the A to Z and MIRACL trials the reduction in low density lipoprotein (LDL) concentrations were 1.6 mmol/l, but whereas MIRACL confirmed the benefit of 80 mg atorvastatin in the first four months after an ACS, A to Z showed no such benefit with 80 mg of simvastatin. One noticeable difference between A to Z and the MIRACL and PROVE-IT studies was that A to Z showed a much smaller decrease in mean C reactive protein concentrations in the treated group (16.7% v 34%), perhaps indicating that the anti-inflammatory role of statins may be the crucial therapeutic mechanism in the early stages after an ACS.

▲ **De Lemos JA**, Blazing MA, Wiviott SD, *et al*. Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes. *JAMA* 2004;292:1307-16.

**Lyse then stent acute MI** ► In patients with ST segment elevated myocardial infarction (STEMI), early post-thrombolysis routine angioplasty has been discouraged because of its association with high incidence of events. The GRACIA-1 trial was designed to reassess the benefits of an early post-thrombolysis interventional approach in the era of stents and new antiplatelet agents. All 500 patients with thrombolysed STEMI (with recombinant tissue plasminogen activator) were randomly assigned to angiography > 24 hours after thrombolysis, or to an ischaemia guided conservative approach. The primary end point was the combined rate of death, reinfarction, or revascularisation at 12 months. Invasive treatment included stenting of the culprit artery in 80% (199 of 248) patients, bypass surgery in six (2%), non-culprit artery stenting in three, and no intervention in 40 (16%). PredischARGE revascularisation was needed in 51 of 252 patients in the conservative group. By comparison with patients receiving conservative treatment, by one year, patients in the invasive group had lower frequency of primary end point (23 (9%) v 51 (21%), risk ratio (RR) 0.44, 95% CI 0.28 to 0.70;  $p = 0.0008$ ), and they tended to have reduced rate of death or reinfarction (7% v 12%, RR 0.59, 95% CI 0.33 to 1.05;  $p = 0.07$ ). At 30 days both groups had a similar incidence of cardiac events. In-hospital incidence of revascularisation induced by spontaneous recurrence of ischaemia was higher in patients in the conservative group than in those in the invasive group. How this strategy compares to primary percutaneous intervention ("stent" rather than "lyse then stent") is not yet clear.

▲ **Fernandez-Avilés F**, Alonso JJ, Castro-Beiras A, *et al* on behalf of the GRACIA (Grupo de Análisis de la Cardiopatía Isquémica Aguda) Group. Routine invasive strategy within 24 hours of thrombolysis versus ischaemia-guided conservative approach for acute myocardial infarction with ST-segment elevation (GRACIA-1): a randomised controlled trial. *Lancet* 2004;364:1045-53.

**You can be fat and fit** ► Obesity is a well known risk factor for coronary heart disease. However, most studies investigating this have not adequately measured physical activity and functional capacity. Thus the WISE (women's ischemia syndrome evaluation) study set out to investigate the relation between measures of obesity, physical fitness, and coronary artery disease (CAD) risk factors, angiographic disease, and adverse cardiovascular events. A total of 906 women with clinical indications for coronary angiography following an acute presentation to hospital were recruited to the study, and followed up for a mean of 3.9 years for adverse outcomes. Overall, 76% of the women were found to be overweight (body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup>), 70% had poor functional capacity (Duke activity status index < 25), and 39% had obstructive CAD. As expected overweight women were more likely to have traditional CAD risk factors, but neither BMI nor abdominal obesity measures were significantly associated with obstructive CAD or future adverse cardiovascular events after adjusting for other risk factors ( $p = 0.05$  to 0.88). On the other hand, those with low activity scores were significantly more likely to have CAD risk factors and obstructive CAD (44% v 26%,  $p < 0.001$ ). The authors suggest that fitness may be more important than being overweight or obese for cardiovascular risk in women, and that evaluation of physical activity should therefore form an integral part of cardiovascular risk stratification.

▲ **Wessel TR**, Arant CB, Olson MB, *et al*. Relationship of physical fitness vs body mass index with coronary artery disease and cardiovascular events in women. *JAMA* 2004;292:1179-87.

**VALIANT suggests renal impairment without creatinine rise is bad for you** ► As part of VALIANT (valsartan in acute myocardial infarction trial), 14 527 patients with acute MI complicated by clinical or radiologic signs of heart failure or left ventricular dysfunction were studied. The risk of death or the composite end point of death from cardiovascular causes, reinfarction, congestive heart failure, stroke, or resuscitation after cardiac arrest increased with declining estimated glomerular filtration rates (GFRs). Although the rate of renal events increased with declining estimated GFRs, the adverse outcomes were predominantly cardiovascular. Below 81.0 ml/min/1.73 m<sup>2</sup>, each reduction of the estimated GFR by 10 units was associated with a hazard ratio for death and non-fatal cardiovascular outcomes of 1.10 (95% CI 1.08 to 1.12), which was independent of the treatment assignment. Nearly 22% of the population had renal impairment (GFR < 60 ml/min/1.73 m<sup>2</sup>).

▲ **Anavekar NS**, McMurray JJV, Velazquez EJ, Solomon SD, Kober L, Rouleau J-L, White HD, Nordlander R, Maggioni A, Dickstein K, Zelenkofske S, Leimberger JD, Califf RM, Pfeffer MA. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med* 2004;351:1285-95.

## HEART FAILURE

**Tai chi: mind over heart failure** ► Thirty patients with chronic stable heart failure and left ventricular ejection fraction  $\leq 40\%$  (mean (SD) age 64 (13) years; mean baseline ejection fraction 23 (7)%; median New York Heart Association functional class II, range I-IV) were randomly assigned to receive usual care ( $n = 15$ ), which included pharmacologic treatment and dietary and exercise counselling, or 12 weeks of tai chi training ( $n = 15$ ) in addition to usual care. Tai chi training consisted of a one hour class held twice weekly. At 12 weeks, patients in the tai chi group showed improved quality of life scores (mean between group difference in change -25 points,  $p = 0.001$ ), increased distance walked in six minutes (135 m,  $p = 0.001$ ), and decreased serum B type natriuretic peptide concentrations (-138 pg/ml,  $p = 0.03$ ) compared with patients in the control group. A trend towards improvement was seen in peak oxygen uptake. No differences were detected in catecholamine concentrations. Tai chi may be a beneficial adjunctive treatment that enhances quality of life and functional capacity in patients with chronic heart failure who are already receiving standard medical treatment.

▲ **Yeh GY**, Wood MJ, Lorell BH, Stevenson LW, Eisenberg DM, Wayne PM, Goldberger AL, Davis RB, Phillips RS. Effects of tai chi mind-body movement therapy on functional status and exercise capacity in patients with chronic heart failure: a randomized controlled trial. *Am J Med* 2004;**117**:541–8.

## GENERAL CARDIOLOGY

**Statins reduce stroke risk** ► A search yielded 65 trials with 200 607 patients for a meta-analysis to determine whether treatment effects differed between types of lipid lowering interventions and between patient samples with and without coronary heart disease. The risk ratio for non-fatal and fatal stroke for statins as compared with control interventions was 0.82 (95% CI 0.76 to 0.90). The corresponding risk ratios for statins as compared with control were 0.75 (95% CI 0.65 to 0.87) for patients with coronary heart disease and 0.77 (95% CI 0.62 to 0.95) for those without coronary heart disease. The confidence intervals of risk ratios for non-fatal and fatal stroke associated with fibrates, resins, n-3 fatty acids, and diet all included 1, as did the confidence intervals for these interventions in patients with and without coronary heart disease. Weighted meta-regression analysis suggested a stronger association of stroke reduction with statin treatment than with the extent of cholesterol reduction.

▲ **Briel M**, Studer M, Glass TR, Bucher HC. Effects of statins on stroke prevention in patients with and without coronary heart disease: a meta-analysis of randomized controlled trials. *Am J Med* 2004;**117**:596–606.

**Any HbA<sub>1c</sub> elevation is bad news** ► In 4662 men and 5570 women, haemoglobin (Hb) A<sub>1c</sub> and cardiovascular disease events and mortality were assessed during the follow up period to 2003. Persons with HbA<sub>1c</sub> concentrations less than 5% had the lowest rates of cardiovascular disease and mortality. An increase in HbA<sub>1c</sub> of 1 percentage point was associated with a relative risk for death from any cause of 1.24 (95% CI 1.14 to 1.34;  $p < 0.001$ ) in men and with a relative risk of 1.28 (95% CI 1.06 to 1.32;  $p < 0.001$ ) in women. These relative risks were independent of age, body mass index, waist-to-hip ratio, systolic blood pressure, serum cholesterol concentration, cigarette smoking, and history of cardiovascular disease. Fifteen per cent of the deaths in the sample occurred in persons with diabetes (4% of the sample), but 72% (375 of 521) occurred in persons with HbA<sub>1c</sub> concentrations between 5–6.9%. Whether HbA<sub>1c</sub> concentrations and cardiovascular disease are causally related cannot be concluded from an observational study;

intervention studies are needed to determine whether decreasing HbA<sub>1c</sub> concentrations would reduce cardiovascular disease.

▲ **Khaw KT**, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A<sub>1c</sub> with cardiovascular disease and mortality in adults: the European prospective investigation into cancer in Norfolk. *Ann Intern Med* 2004;**141**:413–20.

## SAPPHIRE shows the benefits of carotid artery stenting

► In a randomised trial, carotid artery stenting (CAS) with the use of an emboli protection device was compared to endarterectomy (CEA) in 334 patients with coexisting conditions that potentially increased the risk posed by CEA. Patients had either a symptomatic carotid artery stenosis of  $> 50\%$  or an asymptomatic stenosis of  $> 80\%$ . The primary end point of the study was the cumulative incidence of a major cardiovascular event at 1 year—a composite of death, stroke, or myocardial infarction within 30 days after the intervention or death or ipsilateral stroke between 31 days and one year. The study was designed to test the hypothesis that the less invasive strategy, stenting, was not inferior to endarterectomy. The primary end point was reached in 12.2% of the CAS group versus 20.1% in the CEA groups:  $-7.9$  percentage points, 95% CI  $-16.4$  to  $0.7$  percentage points;  $p = 0.004$  for non-inferiority and  $p = 0.053$  for superiority). At one year, carotid revascularisation was repeated in fewer patients who had received stents than in those who had undergone endarterectomy (cumulative incidence  $0.6\%$  v  $4.3\%$ ;  $p = 0.04$ ).

▲ **Yadav JS**, Wholey MH, Kuntz RE, et al for the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;**351**:1493–501.

## Journals scanned

American Journal of Medicine; American Journal of Physiology: Heart and Circulatory Physiology; Annals of Emergency Medicine; Annals of Thoracic Surgery; Archives of Internal Medicine; BMJ; Chest; European Journal of Cardiothoracic Surgery; Lancet; JAMA; Journal of Clinical Investigation; Journal of Diabetes and its Complications; Journal of Immunology; Journal of Thoracic and Cardiovascular Surgery; Nature Medicine; New England Journal of Medicine; Pharmacoeconomics; Thorax

## Reviewers

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